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Award Number: DAMD17-02-1-0223

TITLE: Dynamic Tissue Culture System from Prostate Biopsy Specimens as a Model for Predicting Tumor Radio-sensitivity to Ionizing Radiation Treatments

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REPORT DATE: April 2007

TYPE OF REPORT: Final Addendum

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
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1. REPORT DATE (DD-MM-YYYY) 01-04-2007		2. REPORT TYPE Final Addendum		3. DATES COVERED (From - To) 1 APR 2005 - 31 MAR 2007	
4. TITLE AND SUBTITLE Dynamic Tissue Culture System from Prostate Biopsy Specimens as a Model for Predicting Tumor Radio-sensitivity to Ionizing Radiation Treatments				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER DAMD17-02-1-0223	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Jonathan Walker, M.D. E-Mail: walkerj1@email.arizona.edu				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of Arizona Tucson, AZ 85733-4390				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT The underlying hypothesis driving this project is the notion that all prostate carcinomas are not the same (even if they have the same clinical stage, Gleason score, and pretreatment PSA). By studying individual tumor specimens from patient's prostate carcinomas prior to treatment, it will be possible to obtain information that will make it possible to understand the pathologic factors and molecular regulators that are involved in determining radiation induced apoptosis and intrinsic radio-sensitivity. Our long term goal, for which this proposal will be the first stop, is to develop a system to better individualize each patient's treatment based on various clinical, pathological and molecular biological parameters, thereby maximizing the treatment potential benefit to the patient, while also minimizing the potential treatment toxicity to the patient					
15. SUBJECT TERMS No subject terms were provided.					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	5	19b. TELEPHONE NUMBER (include area code)

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Introduction

The underlying hypothesis driving this project is the notion that all prostate carcinomas are not the same (even if they have the same clinical stage, Gleason score, and pretreatment PSA). By studying individual tumor specimens from patient's prostate carcinomas prior to treatment, it will be possible to obtain information that will make it possible to understand the pathologic factors and molecular regulators that are involved in determining radiation induced apoptosis and intrinsic radio-sensitivity. Our long term goal, for which this proposal will be the first step, is to develop a system to better individualize each patient's treatment based on various clinical, pathological and molecular biological parameters, thereby maximizing the treatment potential benefit to the patient, while also minimizing the potential treatment toxicity to the patient

Body

Study Design: Specific Aim 1 will utilize tissue culture techniques and molecular biology knowledge to develop and optimize a dynamic tissue culture system to obtain and maintain human prostate carcinoma biopsy specimens *in vitro* for up to 72 hours. Specific Aim 2 will utilize molecular biology, immunohistochemistry and radiobiology approaches to evaluate the impact of various molecular regulators of apoptosis on intrinsic radio-sensitivity and tumor response to treatment with prostate brachytherapy.

Specific Aims: 1) Establish a dynamic tissue culture system for prostate biopsy specimens

Specific Aim 1 has been addressed in prior annual reports and thus I will not address this now.

2) Assess the role of p53, bcl-2, and NFkB in determining radiation induced apoptosis, and intrinsic radio-sensitivity the biopsy specimens maintained in a dynamic tissue culture system, as well as the clinical tumor response that is achieved in patients undergoing a curative course of radiation treatments.

- A) Assess the intracellular levels of various molecular regulators of apoptosis and cell death in biopsy specimens obtained from patients with prostate carcinoma
- B) Determine the association between p53, bcl-2, and NFkB and established clinical and pathologic prognostic factors.
- C) Assess the role of p53, bcl-2, and NFkB in determining the extent of radiation induced apoptosis and the intrinsic radio-sensitivity of the biopsy specimens.
- D) Determine the impact of modulating the intracellular levels of p53 and NFkB, on the radio-sensitivity of the biopsy specimens.
- E) Determine the impact of the above studies on the clinical tumor response that is achieved in patients undergoing radiation treatments.

Accomplishments since last report: Since last report we were able to have IRB approval and we were actively obtaining specimens and performing the appropriate radiation treatment. The specimens were being processed and stored for their final immuno-staining once all the specimens had been obtained. I had realized that we would need more time to finish the plans experiments when I received notification from Sponsor Projects that they would be sending the grant back to the DOD. Clearly I was quite taken back by this given that I was activity working on IRB extensions and a DOD extension. Unfortunately when my tech realized that the grant was closing he quickly left thus no further activity was done. Given that all of the immuno-staining was to be done at the end we have no results that are reportable or publishable at this time.

Nota Bene

My formal apology to the Army and the DOD. The delay of this document was to due to my institution's lack of support provided to this investigator. Being a physician scientist at this institution is an insurmountable task between the required clinical responsibilities, the overbearing taxes from the university and the lack of support to the college of medicine and finally not having a department chair makes the situation untenable. I have made attempts to discuss this with university administration (including the VPR) significantly earlier in this affair however my requests were rejected. Again I apologize for the delay clearly I understand that the DOD will hold

me low regard in the future. However I would hope that the DOD would see that the lack of institutional support, and that this project was clearly doomed before I became involved. Also I would hope that the DOD will realize there is more than enough blame to be placed on all involved and the that this investigator is not solely responsible for the end result.

In closing an unfortunate situation exist at this institution such that this research project was doomed from the start given the multiple changes in the PI. Despite my attempts to complete this project, it was severely hindered by this institution. In retrospect I should have never agree to become responsible for this project. I now have a better understanding the environment here and the significant issues associated with this grant when I became involved and thus I should have never agreed to taken it on for it has hindered my other projects and had been an excessive burden.

Key Research Accomplishments

This project has been approved by the IRB ands we were able to procure and grow tissue for radiation treatment.

Reportable Outcomes

We have no reportable outcomes at this time.

Conclusions

We were able to grow biopsy specimens in an organ culture model. The organ culture specimens could be irradiated and this model can be used to determine tissue changes associated with irradiation though we were not able to show this here due to a lack off time.

References

None at this time.

Appendices

None at this time.